Dear friends of clinical journal club - load the file down at https://www.mdc-berlin.de/cjc. This website also gives you access to my seminar on Wednesdays 16:00 English and 17:00 German. You need to click on *Besprechung beizutreten*. If it fails to work immediately, keep on clicking.

A 76-year-old man with coronary artery disease and heart failure with reduced ejection fraction presented to clinic with an 8-month history of progressive breast enlargement and tenderness. Which of the following is most likely to identify the underlying etiology of this finding? You are offered four strategies: Computed tomography of the chest, abdomen, and pelvis, Measurement of serum testosterone level, Medication review, Screening for substance use, and Testicular examination. This quiz is easy! Hypokalemia and even low-normal plasma potassium levels increase the risk of ventricular arrhythmias among patients with cardiovascular disease. An assessment of a strategy of actively increasing plasma potassium levels to the high-normal range is needed. In a multicenter, open-label, event-driven, randomized superiority trial, investigators enrolled participants at high risk for ventricular arrhythmias (defined as those with an implantable cardioverter–defibrillator [ICD]) and with a baseline plasma potassium level of 4.3 mmol per liter or lower. Participants were randomly assigned, in a 1:1 ratio, to a treatment regimen aimed at increasing the plasma potassium level to a high-normal level (4.5 to 5.0 mmol per liter) by means of potassium supplementation, a mineralocorticoid receptor antagonist, or both plus dietary guidance and standard care (high-normal potassium group) or to standard care only (standard-care group). The primary end point was a composite of documented sustained ventricular tachycardia or appropriate ICD therapy, unplanned hospitalization (>24 hours) for arrhythmia or heart failure, or death from any cause, assessed in a time-to-first-event analysis. Not surprisingly, keeping potassium values up reduced events. Among older adults with frailty, evidence on the benefits and risks of discontinuing antihypertensive drugs is limited. Investigators assigned, in a 1:1 ratio, nursing home residents 80 years of age or older who were receiving more than one antihypertensive drug and had a systolic blood pressure below 130 mm Hg to a protocol-driven strategy of progressive reduction of antihypertensive treatment (step-down group) or to receive usual care (usual-care group). Patients were to be followed for up to 4 years. The primary end point was death from any cause. Reducing

medications caused no harm. However, no obvious benefits (less falls etc.) were observed. Influenza remains a major health burden despite the use of licensed vaccines. Nucleoside-modified messenger RNA (modRNA) influenza vaccines have shown promising immunogenicity against influenza and an acceptable safety profile in a phase 1–2 trial. Investigators compared modRNA vaccine against conventional inactivated quadrivalent influenza vaccine (control). The modRNA vaccine had greater efficacy. Thus, the modRNA vaccine was better than the conventional vaccine. Pheochromocytoma and paraganglioma are neoplasms originating in the adrenal medulla and extra-adrenal paraganglia, respectively. Most cases of metastatic pheochromocytoma and paraganglioma are driven by dysregulation of the hypoxia-inducible factor 2α (HIF-2α) pathway. Belzutifan is a HIF-2α inhibitor that may provide antitumor activity in patients with advanced pheochromocytoma or paraganglioma. Investigators conducted a phase 2, international, single-group trial involving 72 participants with locally advanced or metastatic pheochromocytoma or paraganglioma that was not amenable to surgery or curative-intent treatment. Participants received belzutifan at a dose of 120 mg once daily until the occurrence of progression, unacceptable toxic effects, or withdrawal from the trial. The primary end point was confirmed objective response (complete or partial response) as assessed by blinded independent central review. Belzutifan showed antitumor activity with durable responses in participants with advanced pheochromocytoma or paraganglioma. The N Engl J Med review covers the long QT syndrome. The mystery patient of the week is a young man with bizarre behavior, confusion, and a seizure. In the Lancet, we confront influenza once more. A randomized trial of high-dose versus low-dose influenza vaccine was conducted. High-dose offered more protection than low-dose influenza vaccine. SJörgen's s syndrome is an auto-immune diseases featuring dry-eyes, dry mouth and affects lung, nerves and kidneys. Anti-Ro and anti-La antibodies are common. The neonatal Fc receptor (Fc-Rn) recycles antibodies, including auto-antibodies, and prolongs their lifespans. Nipocalimab is an antibody directed against Fc-Rn. Nipocalimab was tested in Sjörgen's syndrome patients and led to improved outcomes. Dapagliflozin (SGLT2 inhibitor) improves outcomes for chronic kidney disease (CKD) patients. In a randomized trial, the mineralocorticoid receptor blocker, balcinrenone, lead to additional improvement. Then, the Global Burden of Disease

study underscores the role of CKD, as of 2023 and predicts future relevance. Lancet reviews postpartum cardiomyopathy. Lancet also discusses non-celiac gluten sensitivity (NCGS), a condition that may explain some of “functional” bowel disease. Science Magazine draws attention to Aerolysin, a toxin which forms pores in resident macrophage target cells and could be responsible for inflammatory bowel disease. Aerolysin is formed by the bacterial strain, *Aeromonas sp*. Washington Post reports that embracing new technologies may help aging persons stay mentally fit and protect from mental decline. Join me on November 26 for the above and more in another stunning, orally presented, clinical journal club, 16:00 in English and 17:00 in German.
Sincerely, Fred Luft

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